

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of : Jansson Examiner: David Lukton
Serial No. : 10/530,866 Art Unit: 1654
Filed : April 11, 2005 Attorney's docket: JANSSON7
Title : Use of Grelin for treating malnutrition in gastrectomized individuals

DECLARATION BY John-Olov Jansson 37 C.F.R. § 1.132

I, John-Olov Jansson declare and state as follows:

1. I am the named inventor of the present invention.
2. I have read and understood the present application and the current claim of said application. I have reviewed the office action dated October 29, 2007 and the office action dated May 21, 2007.
3. I hereby provide further information regarding the experiments described in the above mentioned application and some further information regarding gastrectomy surgery.
4. The data presented in the application figure 1 and 2 was obtained with 5-6 rats per group.
5. The data are summarized in the following table.

Food/energy consumption	At own initiative			
		Displayed increased desire for food.		Displayed increased desire for food.
Surgical treatment	Sham operated (surgical procedure and anesthesia but no removal of stomach)		Gastrectomized	
Treatment	Administration is initiated 4 weeks after surgery and continued for 2 weeks			
	Water	MK677 (4 mg/kg/day)	Water	MK677 (4 mg/kg/day)
Weight gain	20.2 +/- 2.4 g	25.6 +/- 3.9 g	13.6 +/- 2.0 g	19.6 +/- 2.0 g
Sum fat pad weight			13.1 g	16 g

Table 1.

6. These data demonstrate that MK677 treatment normalizes the weight gain in gastrectomized individuals, as the weight gain in MK677 treated gastrectomized individuals equals the weight gain in sham operated individuals receiving water.
7. By comparing the weight of fat pads in the water treated rats (13,1 g) and in the MK677 treated rats (16.0) (Fig 2 and table 1 above) an increase of 22% can be calculated. This difference is significant (* $P < 0.05$, as indicated in Fig 2; calculated with Student's t-test). Calculation using the weight gain observed leads to an increase of 44.1 %, which is significant as well. The fat pad mass can only be measured once for each animal e.g. at the time of sacrifice of the animal, therefore no information regarding the increase of fat pad mass during the treatment period is available. However, the fact that the fat pad weight at the time of sacrifice was 22 % higher in the ghrelin analogue treated animals compared to the water vehicle treated controls shows that the ghrelin analogue has a significant stimulatory effect on body fat.
8. Comparison between drug treated and vehicle treated individuals is an established way to determine if a drug is effective. Therefore, it can be concluded that ghrelin analogues enhance body fat weight in gastrectomized rats.
9. MK677 is a representative ghrelin analogue. Like ghrelin itself, MK-0677 binds to the classic ghrelin receptor GSR-1a, which actually was identified, based on its capacity to bind to MK-0677. Like ghrelin, MK-0677 exerts anabolic effects in several species, including man and mice (Smith R et al Horm Res 51 Suppl 3:1-8, 1999; Camina JP et al Endocrine 22:5-12, 2003; Sun Y et al Proc Natl Acad Sci U S A. 101:4679-4684, 2004).
10. In the cause of performing a gastrectomy a vagotomy may occur. For practical reason, about 99 % of all gastrectomies are accompanied by a subdiaphragmal vagotomy due to the fact that it is very difficult to avoid the latter surgical procedure (Schwartz's Principles of Surgery: A Modern Approach, Edition 8, Ed: FC Bruncardi et al 2004 Chapter 25).
11. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of United States Code and that such wilful false statements may jeopardize the validity of the application any patent issued thereon.

Date: January 29, 2008

Signature: _____


(John-Olov Jansson)